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SYSTEMATIC REVIEWS

Cost-Utility Analyses in Diabetes: A Systematic Review and Implications from Real-World Evidence

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ABSTRACT

Objectives: To systematically review the cost-effectiveness of diabetes interventions, identify high-value diabetes services, and estimate potential gains from increasing their utilization. **Methods:** The study consisted of two steps. First, we reviewed cost-utility analyses (CUAs) related to diabetes published through the end of 2012, using the Tufts Medical Center Cost-Effectiveness Analysis Registry (www.cearegistry.org). We used logistic regression to examine factors independently associated with favorable cost-effective ratios. Second, we used the Humedica electronic medical records to estimate potential savings and health benefits gained by shifting patients currently receiving low-value services to high-value alternatives. **Results:** We identified 196 diabetes CUAs, of which 55% examined pharmaceuticals. Most (70%) diabetes CUAs focused on treatment rather than prevention. Most used a health care payer perspective and were industry-sponsored. Of the 497 published cost-utility ratios, 82% examined an intervention recommended by diabetes guidelines. Approximately 73% of the interventions were cost-saving or below $50,000 per quality-adjusted life-year. Logistic regression analysis showed that higher-quality CUAs, CUAs conducted from the US perspective, surgical interventions, and guideline-recommended interventions were more likely to report favorable ratios. Of the 7907 eligible patients with diabetes in our sample, up to 7117 could in principle be shifted to cost-saving treatments, reducing costs by $12.5 million and gaining more than 1938 quality-adjusted life-years over a lifetime. **Conclusions:** Most diabetes interventions evaluated by CUAs are recommended by practice guidelines and may provide good value for money. Our results indicate that patients with diabetes and the health care system could potentially benefit from shifting to the greater use of high-value services.

Keywords: cost-utility analysis, diabetes, health care utilization, systematic review.

Introduction

It is well documented that diabetes places a substantial economic burden on patients and the health care system [1–3]. In the United States, costs associated with prediabetes and diabetes have increased from $174 billion in 2007 to $245 billion in 2012, including $176 billion direct medical costs and $69 billion indirect costs due to related disability and lost productivity [1]. Spending on diabetes accounts for more than one in five US health care dollars and, on average, people with diabetes spend 2.3 times more on health care services [1,2]. Diabetes also imposes a substantial burden on patients' quality of life and reduces life expectancy because it increases the risk of chronic complications, such as cardiovascular diseases, kidney diseases, and eye and foot problems [3]. It is one of the top 10 leading causes of death in the United States, and the number of afflicted patients has increased substantially in the past 5 years, from 17.5 million in 2007 to 22.3 million in 2011 [2].

Cost-effectiveness analysis (CEA) is a widely used methodology for assessing the value of health care interventions. CEA compares a health care intervention to a comparator, reporting the intervention's performance in the form of an incremental cost-effectiveness ratio (ICER). The ICER's numerator represents the intervention's incremental cost, whereas the ICER's denominator represents its incremental health benefit. A small ICER indicates that the intervention is favorable because it indicates that it produces health units of health inexpensively. A CEA may also find that an intervention is "cost-saving" (reduces costs and improves health) or that it is "dominated" (increases costs and makes health worse).

Several systematic reviews have surveyed the diabetes intervention CEA literature [4–8]. Klonoff and Schwartz [4] reviewed

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CEAs on 17 widely practiced diabetes interventions and found that most interventions were cost-saving or cost-effective. Zhang et al. [5] updated this study by adding CEAs on diabetes prevention and screening, as well as studies on the economic cost of diabetes. They emphasized the importance of efficiently using resources on cost-effective interventions. Raikou and McGuire [6] and Vijgen et al. [7] reviewed economic evaluations of interventions for type 2 diabetes. A more recent review by Li et al. [8] described 56 CEAs published through 2008 that evaluated interventions recommended by the American Diabetes Association (ADA) to prevent and control diabetes. They concluded that preventive interventions were cost saving or highly cost-effective and hence should be prioritized by policymakers.

Compared with earlier studies, this analysis is more comprehensive, reviewing a total of 196 articles, providing more detailed information on the articles reviewed, and placing these findings in broader perspective by using real-world data to demonstrate savings at the health care system level. Our study is composed of a systematic review and a "what-if" analysis. First, we systematically review cost-utility analyses (CUAs), a subgroup of CEAs that quantify health benefits in terms of quality-adjusted life-years (QALYs). A QALY is a generic measure that reflects both length of life and morbidity. It has been used in studies evaluating interventions addressing a wide range of health conditions [9]. Our analysis covers diabetes-related CUAs published in peer-reviewed, English-language journals through 2012. As part of this review, we also examine factors associated with favorable cost-effectiveness. Second, we identify "high-value" diabetes services (e.g., cost-saving) and estimate potential gains from increasing their utilization. The purpose was to assess the impact of hypothetical resource reallocation scenarios on costs and health benefits gained. We acknowledge at the outset that this is an exploratory analysis, and the main objective was to demonstrate potential gains from optimal use of high-value services and to show applications of CUAs using real-world data.

Methods

Step 1: Systematic Review

Data: The Tufts Medical Center Cost-Effectiveness Analysis Registry

We analyzed information on CUAs cataloged in the Tufts Medical Center Cost-Effectiveness Analysis Registry (available at http://www.cearegistry.org), a comprehensive database with more than 3600 CUAs and 9800 cost-utility ratios published in the peer-reviewed literature from 1976 through the end of 2012. The registry contains information extracted from CUA articles published in English. The registry researchers identify articles for inclusion in the registry by searching MEDLINE using the keywords "QALY," "quality-adjusted," and "cost-utility analysis." Two trained readers independently review all articles to be included in the registry (see Appendix 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.12.004 for more details of search strategies). The readers summarize the study methodology, the reported cost-effectiveness ratios, and all utility weights used in the article [10–15]. Registry ICERs are standardized so that they are expressed in terms of 2012 US dollars.

We included Tufts registry articles pertaining to any of the following three disease categories: diabetes mellitus, endocrine disorders, and other disorders. We then reviewed the titles and abstracts and selected articles focusing on diabetes-related interventions. Selected interventions covered type 1 diabetes, type 2 diabetes, gestational diabetes mellitus, and complications of diabetes. Only those CUAs that correctly conducted incremental analyses were included. We excluded reviews, editorials, and other types of economic studies such as cost-benefit analysis and CEAs using other health measures (e.g., hemoglobin A_{1c} level).

Analysis: Systematic review of diabetes CUAs

We reported the results of the systematic review in two ways. First, we summarized the study characteristics. We grouped the articles on the basis of prevention stage: *primary prevention* (interventions that protect healthy people from the onset of diabetes and its complications), *secondary prevention* (interventions that mitigate the progression of diabetes and its complications during the early stages of the disease), and *tertiary prevention* (interventions that treat or manage patients with diabetes). We recorded the following key study features: 1) publication year; (2) country of study (the country to which the results are applied); 3) type of study funding or sponsorship (industry, nonindustry, unfunded, or not specified); 4) intervention type (e.g., pharmaceutical, screening, medical device, or surgical); 5) the analytic perspective (societal, health care payer, or other); 6) whether the study explicitly and clearly specified the analytic time horizon, the intervention, the comparator, and the target population; 7) whether the study conducted a sensitivity analysis; 8) evaluation of the study's overall quality (scored 1–7); and 9) whether the intervention was recommended by either the 2011 American Association of Clinical Endocrinologists (AACE) medical guidelines [16] or the 2012 ADA standards of medical care in diabetes [17]. Study quality was evaluated on the basis of factors such as the reasonableness of assumption, overall presentation quality, the completeness and clarity of methods, including the model used, data sources, costs, utility, ratios, and characterization of uncertainty.

The second set of analyses examined the distribution of ICERs. We classified ICERs as cost-saving (less costly, more effective)—less than $20,000/QALY, $20,000 to $50,000/QALY, $50,000 to $100,000/QALY, $100,000 to $200,000/QALY, more than $200,000/QALY—and dominated (more costly, less effective), similar to the classification used by Li et al. [8]. We used logistic regression to investigate whether ratio favorability (e.g., having a value less than the median for all diabetes-related ICERs) is predicted by variables such as country (US vs. non-US), type of sponsorship, intervention type, prevention stage, study perspective (societal vs. nonsocietal), study quality (dichotomized), or whether the intervention is recommended by either the 2011 AACE guidelines or the 2012 ADA standards. The analysis assigned each ratio a statistical weight of $1/n$, where n was the number of ratios reported by that ratio's article. This approach ensures that no single article disproportionately affects the results by virtue of its reporting a large number of ratios [18].

Step 2: Resource Reallocation Scenarios

Data: Humedica electronic medical records

We used the 2008-2012 Humedica electronic medical record (EMR) data sets to help quantify the utilization of various diabetes-related services identified in the Tufts Medical Center Cost-Effectiveness Analysis Registry as providing good value for money. Humedica is one of the largest EMR databases in the United States that includes clinical and health care utilization data from a network of provider organizations covering nearly 30 million patients across 38 states (www.humedica.com). It is a patient-level clinical data set that combines encounter data, clinical details, and prescription records in patients' EMRs. As described below, we used the Humedica EMR data to estimate intervention utilization rates, and identified around 400,000 patients in the Humedica EMR with diagnoses of diabetes, including type 1 diabetes (3%), type 2 diabetes (53%), and other types of diabetes (prediabetes, gestational diabetes mellitus, and unknown diabetes type) (44%).

Analysis: Potential gains from shifting patients to cost-saving interventions

We used the Humedica EMR data to estimate the potential number of patients who could be switched to high-value (cost-saving) diabetes services and treatments identified in our review of the Tufts Medical Center Cost-Effectiveness Analysis Registry and recommended by the AACE guidelines or the ADA standards. We assumed that patients were candidates for these high-value services if the Humedica data indicated that they were currently using a substitute diabetes-related service that achieved inferior health outcomes (fewer QALYs) at a higher cost.

From the US health care payer perspective, we estimated potential cost savings and QALY gains by simulating a hypothetical shift of these patients to high-value interventions. Recognizing that not all patients would in reality be eligible because services must be tailored to avoid adverse drug events, we explored the implications of shifting a range of appropriate patients using low-value interventions (10%–90%) [19]. We also reviewed the comparative effectiveness research (CER) literature to ensure that there was clinical evidence to support the idea that these shifts could be accomplished safely and that they would improve effectiveness.

We estimated total savings as the product of the number of patients shifted to the new intervention and the per-person reduction in lifetime costs. Similarly, we estimated total health gain as the product of the size of this population and the per-person lifetime QALY gains. Per- person cost savings and QALY gains came from the CUA studies, with cost estimates based on direct medical costs only. We standardized all costs by converting them to 2012 US dollars. All analyses were performed using SAS, version 9.3 (Cary, NC).

Results

Step 1: Characteristics of Diabetes-Related CUAs

We identified 312 CUAs on endocrine disorders in the registry. One hundred sixteen articles were excluded because they either pertained to endocrine disorders other than diabetes or did not report a valid ratio. The final sample included 196 articles and 497 ICERs (see Appendix 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.12.004 for a reference list of 196 diabetes CUAs) (Fig. 1). The annual number of diabetes CUA publications increased markedly over time, from 7 published before 1997 to 120 published from 2008 to 2012 (Table 1). Most diabetes CUAs focused on tertiary prevention (n = 138, 70%). The published articles were from more than 20 countries, of which 41% (n = 80) were US-based. The most commonly assessed diabetes interventions included pharmaceuticals (n = 107, 55%), health education programs (n = 34, 17%), and delivery of care (n = 33, 17%). Most (n = 140, 71%) of the CUAs presented results from the health care payer perspective, regardless of prevention stage. Industry was the most common source of funding among studies evaluating secondary (n = 21, 49%) and tertiary (n = 79, 57%) prevention measures. In contrast, of the 15 studies evaluating primary prevention, more than half (n = 9, 60%) reported nonindustry sponsorship, whereas the rest (n = 4, 27%) did not disclose their sponsorship.

As recommended by CEA guidelines [10–15], most of the diabetes CUAs explicitly specified the time horizon (n = 188, 96%), the intervention (n = 192, 98%), the comparator (n = 190, 97%), and the target population (n = 192, 98 %). A total of 96% (n = 188) of the studies performed sensitivity analyses. The average study quality score was 4.5 for diabetes CUAs, which was slightly higher than the average quality rating (4.4) for all studies in the Tufts Medical Center Cost-Effectiveness Analysis Registry.

Of the 497 published ICERs, 82% (n = 406) evaluated guideline-recommended interventions (e.g., diabetes retinopathy screening). The median value for all diabetes ICERs was roughly $17,200 per QALY gained ($15,400 per QALY gained when weighted by one over the number of ratios reported by each ICER's article) compared with a median of $18,600 per QALY for all studies cataloged in the Tufts Medical Center Cost-Effectiveness Analysis Registry. Industry-sponsored interventions had a much lower (more favorable) median value than did those sponsored by nonindustry entities (roughly $12,400/QALY vs. $ 36,600/QALY). A total of 20% (n = 98) of diabetes-related ICERs were cost saving, 73% (n = 355) were below the most often used threshold of $50,000/QALY, and 6% (n = 30) were dominated (less effective and higher costs) (Fig. 2).

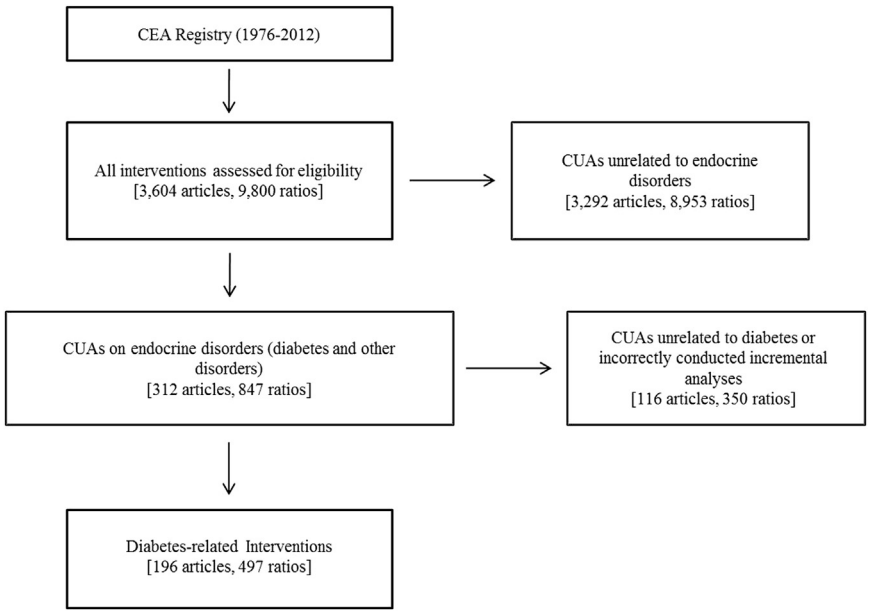

Fig. 1 – Selection of diabetes cost-utility studies for systematic review. CEA, cost-effectiveness analysis; CUA, cost-utility analysis.

Table 1 – Characteristics of cost-utility studies of diabetes interventions.

Characteristic	Primary (n = 15)	Secondary (n = 43)	Tertiary (n = 138)	All studies (n = 196)
Year of publication				
≤1997*	0 (0)	0 (0)	7 (5)	7 (4)
1998–2002	2 (13)	6 (14)	6 (4)	14 (7)
2003–2007	3 (20)	20(47)	32 (23)	55 (28)
2008–2012	10 (67)	17 (40)	93 (67)	120 (61)
Study country				
United States	6 (40)	21 (49)	53 (38)	80 (41)
United Kingdom	1 (7)	6 (14)	26 (19)	33 (17)
Canada	1 (7)	3 (7)	11 (8)	15 (8)
Sweden	1 (7)	2 (5)	7 (5)	10 (5)
The Netherlands	2 (13)	1 (2)	6 (4)	9 (5)
Other	4 (27)	10 (23)	35 (25)	49 (25)
Funding source				
Industry	1 (7)	21 (49)	79 (57)	101 (52)
Nonindustry	9 (60)	13 (30)	31 (22)	53 (27)
No funding	1 (7)	1 (2)	8 (6)	10 (5)
Not disclosed	4 (27)	8 (19)	20 (15)	32 (16)
Type of intervention†				
Pharmaceutical	1 (7)	18 (42)	88 (64)	107 (55)
Health education or behavior	7 (47)	11 (26)	16 (12)	34 (17)
Care delivery	2 (13)	6 (14)	25 (18)	33 (17)
Screening	6 (40)	16 (37)	3 (2)	25 (13)
Surgical	0 (0)	1 (2)	11 (8)	12 (6)
Diagnostic procedure	0 (0)	7 (16)	4 (3)	11 (6)
Medical device	0 (0)	1 (2)	10 (7)	11 (6)
Medical procedure	0 (0)	0 (0)	9 (7)	9 (5)
Other or NA	0 (0)	4 (9)	3 (2)	7 (4)
Immunization	1 (7)	0 (0)	0 (0)	1 (1)
Study perspective				
Health care payer	7 (47)	27 (63)	106 (77)	140 (71)
Societal	6 (40)	11 (26)	15 (11)	32 (16)
Other or not specified	2 (13)	5 (12)	17 (12)	24 (12)
Presentation of				
Time horizon	13 (87)	38 (88)	137 (99)	188 (96)
Intervention	15 (100)	40 (93)	137 (99)	192 (98)
Comparator	15 (100)	39 (91)	136 (99)	190 (97)
Target population	15 (100)	40 (93)	137 (99)	192 (98)
Sensitivity analysis				
Yes	14 (93)	41 (95)	133 (96)	188 (96)

Note. Values are n (%).
CUA, cost-utility analysis; NA, not applicable/available.
* The first diabetes CUA was published in 1994.
† Each article can have more than one intervention, and some interventions may fall under more than one type. Therefore, the percentages may total more than 100.

We used logistic regression to examine the association between each characteristic and the tendency for an ICER to have a lower (e.g., more favorable) value than the sample weighted median of $15,400 per QALY. The results showed, for instance, that ICERs reported by a CUA conducted from a US perspective were more likely to be favorable than other ratios (odds ratio [OR] = 2.82; 95% confidence interval [CI] 1.40–5.70). Interventions recommended by either the 2011 AACE guidelines or the 2012 ADA standards were more likely to report favorable ratios (OR = 2.62; 95% CI 1.03–6.66). Ratios for surgical CUAs were more favorable (OR = 9.01; 95% CI 1.45–55.94) than other ratios. ICERs reported by higher-quality studies (rating score ≥4.5) were more favorable than other ICERs (OR = 2.39; 95% CI 1.19–4.81) after controlling for other factors. Other study characteristics, including sponsorship, prevention stage, study perspective, and nonsurgical interventions, did not independently affect ICERs' favorability.

Step 2: Value of Shifting Patients to High-Value Treatments

Of the interventions considered in this systematic review, 98 were reported to be more effective and less expensive than their comparators. Among these dominant interventions, 67 were recommended by the AACE guidelines or the ADA standards. Because we included studies conducted only from a US perspective, we retained only 15 of the 67 high-value interventions. For our analysis, we finally identified 4 high-value interventions from these 15 interventions that could be evaluated using the Humedica data set, all of which were pharmaceutical treatments (Table 2). (Use of interventions such as lifestyle changes and diabetes-specific nutritional meal replacement could not be directly determined from the Humedica data, given the lack of information on these interventions in the data set.) Among the four selected studies of these interventions, three were sponsored by industry [20–22]. The other study was government-

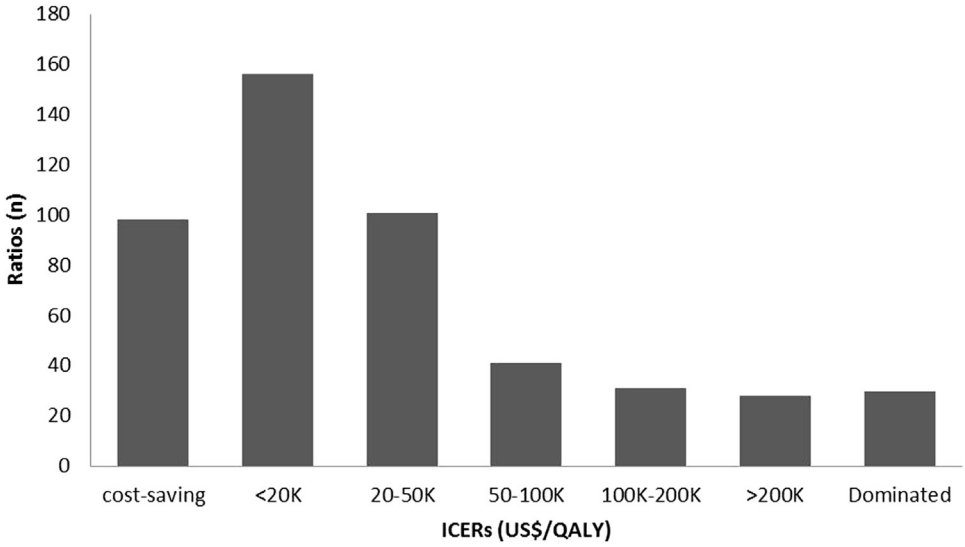

Fig. 2 – Distribution of ICERs (2012 US $). ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

sponsored [23]. The time horizon used in these four studies was either lifetime or 30 years.

Each year, about 41,000 patients in the Humedica data set were diagnosed with type 2 diabetes and hypertension. Approximately 90% (n = 37,593) of them received intensive hypertension control that is deemed cost-saving. Similarly, most patients with type 2 diabetes (89%, n = 13,894) were treated with pioglitazone plus metformin, a reportedly cost-saving therapy when compared with rosiglitazone plus metformin. For patients with type 2 diabetes taking combination therapy of meglitinides (including repaglinide and nateglinide) plus metformin, however, only 55% (n =569) of them were treated with the reportedly cost-saving drugs repaglinide plus metformin. Utilization of the insulin detemir plus insulin aspart, a reportedly cost-saving treatment, was even lower (14%, n = 244) for

Table 2 – Utilization of selected guidelines' recommended cost-saving interventions in US studies using Humedica data sets.

Article	Target population, intervention, and comparator	Humedica (n)	%
Palmer et al. [20]	*Target population*		
	Patients with type 2 diabetes treated with repaglinide or nateglinide plus metformin		
	Intervention	569	54.7
	Repaglinide plus metformin		
	Comparator	472	46.3
	Nateglinide plus metformin		
Valentine et al. [21]	*Target population*		
	Patients with type 1 diabetes treated with insulin detemir or insulin glargine plus insulin aspart		
	Intervention	244	13.6
	Insulin detemir plus insulin aspart		
	Comparator	1,553	86.4
	Insulin glargine plus insulin aspart		
St Charles et al. [22]	*Target population*		
	Patients with type 2 diabetes treated with pioglitazone or rosiglitazone plus metformin		
	Intervention	13,894	89.1
	Pioglitazone plus metformin		
	Comparator	1,704	10.9
	Rosiglitazone plus metformin		
CDC Diabetes Cost-effectiveness Group [23]	*Target population*		
	People with type 2 diabetes and hypertension		
	Intervention	37,593	90.0
	Intensive hypertension control (treatment with angiotensin-converting enzyme inhibitors or β-blockers)		
	Comparator	4,178	10.0
	Moderate hypertension control (treatment with diet or other drugs)		

CDC, Centers for Disease Control and Prevention.

Table 3 – Hypothetical resource reallocation scenarios: potential change in utilization, lifetime cost savings, and QALYs gained.

Intervention	Comparator	Cost savings per person*	QALYs gained per person	Change in utilization	Total cost savings ($ million)*	Total QALYs gained
Repaglinide/ metformin	Nateglinide/ metformin	5115	0.14	47–425	0.24–2.17	6.58–59.50
Insulin detemir/ insulin aspart	Insulin glargine/ insulin aspart	2660	0.06	155–1398	0.41–3.72	9.30–83.88
Pioglitazone/ metformin	Rosiglitazone/ metformin	649	0.19	170–1534	0.11–1.00	32.30–291.46
Intensive hypertension control	Moderate hypertension control	1373	0.40	418–3760	0.57–5.16	167.20–1504.08
Total				790–7117	1.33–12.49	215.38–1938.92

QALY, quality-adjusted life-year.
* In 2012 US $.

patients with type 1 diabetes, whereas most patients with type 1 diabetes (86%, n = 1553) received insulin glargine plus insulin aspart, a therapy with higher costs and lower health benefits. Results from existing CER studies showed that cost-saving treatments also worked better than or at least as well as their counterparts in terms of both clinical efficacy and the avoidance of major adverse drug events [24–28].

Table 3 summarizes potential per-person cost savings and QALY gains for the four cost-saving interventions, as well as the impact of switching eligible patients to these therapies. The most cost-effective intervention was insulin detemir plus insulin aspart, saving $2660 and gaining 0.06 QALY per person. The potential for shifting patients to high-value treatments was greatest for hypertension control therapies; of the 4178 patients with this condition, 3760 patients (90%) could be shifted from moderate hypertension control drugs (dominated treatments) to intensive hypertension control drugs (cost-saving treatments). Across all treatments, as many as an additional 7117 patients could be shifted to high-value treatments (out of 7907 eligible), saving $12.5 million and gaining 1938.9 QALYs over a lifetime.

Discussion

Our study sheds new light on CUAs evaluating treatments for diabetes and its complications, which represent more than 5% of all CUAs published over the years. The number of diabetes-related CUAs published annually has consistently increased during the past several decades. Most have focused on treatment. More than half of the studies in our sample were conducted from a US or UK perspective. Pharmaceutical and medical device companies funded most of secondary and tertiary prevention CUAs, whereas the government and nonprofit organizations were the major funding sources for primary preventive measures. More than half of all published diabetes CUAs evaluated pharmaceutical treatments. Health care delivery, health education, and preventive care programs, however, are more heavily represented in the diabetes CUA literature than in the CUA literature in general [29].

Almost all diabetes-related studies followed guidelines for the design and reporting of CUAs. They stated the study perspective and time horizon, explicitly specified the target population, the intervention, and the comparator, and performed the sensitivity analysis. The average study quality for diabetes CUAs was slightly higher than the corresponding average score for CUAs evaluating interventions for all diseases. Most of the studies evaluated either AACE- or ADA-recommended interventions. The median ICER reported by industry-sponsored CUAs was lower (more favorable) than the corresponding median ICER reported by other CUAs. This result may reflect more likely publication of studies that yield a favorable ratio, or the use of more favorable assumptions when articles are sponsored by manufacturers [30]. Most ICERs were below the threshold of £30,000 (roughly $50,000) per QALY used by the National Institute for Health and Care Excellence [31]. Diabetes CUAs conducted from a US perspective and studies with higher-quality scores were more likely to report favorable ratios.

Although many studies have systematically reviewed economic evaluations of diabetes interventions, our analysis adds to the literature by estimating potential health and monetary gains from shifting more patients to selected guideline-recommended high-value interventions. Of the four high-value (cost-saving) interventions for which we had utilization data from the Humedica EMR data set, only two were used by more than half of the eligible patients.

On the basis of results from both the CER and CUA literature, we developed a simple scenario to evaluate cost savings and health benefit gains switching patients to high-value interventions. Of 7907 eligible patients in our sample, up to 7117 could be shifted to cost-saving treatments, saving more than $12 million and gaining more than 1900 QALYs.

Our study has several limitations. First, we included only cost-utility studies, which use QALYs to measure health outcomes, although CEAs using other clinical measures of effectiveness are also common. Second, our estimates of how many patients were eligible for but not yet receiving high-value diabetes interventions were based on the Humedica EMR data set. Information in this database is limited to care from within Humedica's provider networks. In addition, the data did not contain information on all cost-saving interventions. More complete data or other types of data (e.g., Medicare) may be used in the future to generate more comprehensive estimations. Third, saving estimates from resource reallocation were based on CUAs published between 2002 and 2009. Information on both costs and effectiveness may have changed since then. Fourth, our analysis of potential gains from shifting to high-value services was based in part on results from industry-sponsored studies from the US perspective, which may be biased [30]. We also verified, however, the clinical effectiveness and safety of our high-value interventions by consulting the CER literature. Our results may be applied to other

countries if their guidelines do not differ significantly from American clinical guidelines.

Finally, our results should be interpreted with caution because we assumed a range of patients who could be shifted to these therapies from their currently used lower-value treatments. Our assumption reflects patient tolerance of these high-value therapies, but other factors, such as promotional advertising, ease of administration, and patients' co-payment, might constrain the shift of patients from lower-value to high-value interventions [32,33].

Conclusions

CEAs help to identify high-value services and hence help to optimize health care spending [34–36]. Our findings suggest that most diabetes interventions evaluated by CUAs were recommended by practice guidelines and produced good value for money (e.g., they cost <$50,000 per QALY gained). Our results also indicate that practice is not economically optimal. Both patients and the health care system could benefit from shifting to the greater use of services that have demonstrated greater clinical effectiveness and lower costs. Future research is needed to explore why cost-saving interventions are not fully utilized, and whether there are patient characteristics that can explain or at least predict the continued use of lower-value services.

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Supplemental Materials

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